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EXAMINER	
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ART UNIT	PAPER NUMBER
1654	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/509,405	NATHAN ET AL.	
	Examiner	Art Unit	
	RONALD T. NIEBAUER	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 December 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,18 and 21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,18 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/5/09, 9/18/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/18/09 has been entered.

Applicants amendments and arguments filed 10/7/09 and 12/19/09 are acknowledged and have been fully considered. Any rejection and/or objection not specifically addressed is herein withdrawn.

Applicant's previously elected Group I (claim 2 drawn to in vivo treatment of cell necrosis) and the species of elastase inhibitor III (MeOSuc-Ala-Ala-Pro-Val-CMK) for the elastase inhibitor; neuronal cells as the cell type; dementia as the disease type in the reply filed on 6/19/07. Applicant's election without traverse of the anti-apoptotic agent as z-VAD-fluoromethylketone in the reply filed on 12/29/08 is acknowledged. Applicants note that the elected species of anti-apoptotic agent is not specifically recited in the specification. Since the elected species of z-VAD-fluoromethylketone is not recited in the claims, whether or not the species represents new matter is not addressed at this stage of examination.

As discussed below, the elected species have been found in the prior art and all claims have been rejected either under 102 or 103. Any art that was uncovered in the course of searching for the elected species is also cited herein.

Claims 2,4-17,19-20 have been cancelled.

Claims 1,3,18,21 are under consideration.

Specification

The amendment filed 12/19/09 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: the amendment as set forth on 12/19/09.

Applicant is required to cancel the new matter in the reply to this Office Action.

Page 16,17,18 have been amended to recite that elastase inhibitor III in the absence of KCN had no effect of cell viability.

Lack of Ipsis Verbis Support

The specification is void of any literal support for elastase inhibitor III in the absence of KCN had no effect of cell viability.

Lack of Implicit or Inherent Support

Section 2163 of the MPEP states: 'While there is no in haec verba requirement, newly added claim limitations must be supported in the specification through express, implicit, or inherent disclosure'.

Although the above statement is with respect to claim limitations a similar analysis is employed for analysis of amendments to the specification.

Page 16 has been amended to recite that elastase inhibitor III in the absence of KCN had no effect of cell viability. However, Figure 5B shows that for the control experiment that for no elastase inhibitor and no KCN that the % cell survival is 100%. However, for the control

experiments in which there is elastase inhibitor III and no KCN the % cell survival is ~90%. Thus Figure 5B suggests that elastase inhibitor III alone effects cell survival since it decreases survival from 100% to ~90%. Thus there is no basis to say that elastase inhibitor III in the absence of KCN had no effect on cell viability. In fact, Figure 5B is evidence that elastase inhibitor III alone effects cell survival since it decreases survival from 100% to ~90%.

Further, it is noted that the amendments of 12/19/09 recite 'no effect of cell viability'. However, the amendment on page 17 refers to Figure 9 which measures apoptosis. Apoptosis is not the equivalent of cell viability. An experiment measuring apoptosis would not lead one to make definitive statements about cell viability. Figures 10 and 11 measure necrosis which is not the equivalent of cell viability. Further, it is noted that the amendments to pages 17 recite an absence of KCN. However, the data of Figures 9 and 10 use STS. It is unclear how experiments with and without STS would lead one to make conclusions regarding KCN.

Applicants argue (page 6 12/19/09) that the specification amendment is to eliminate ambiguity and there is no new matter since the results show cell protection against KCN toxicity. However, the specification amendment does in fact include new matter and does not merely correct a typographical error or ambiguity. Although applicants argue that the results show cell protection, the amendments to the specification expressly recite 'had no effect on cell viability'. Cell protection is not the equivalent of 'no effect on cell viability'. Page 16 has been amended to recite that elastase inhibitor III in the absence of KCN had no effect of cell viability. However, Figure 5B shows that for the control experiment that for no elastase inhibitor and no KCN that the % cell survival is 100%. However, for the control experiments in which there is elastase inhibitor III and no KCN the % cell survival is ~90%. Thus Figure 5B suggests that elastase

inhibitor III alone effects cell survival since it decreases survival from 100% to ~90%. Thus there is no basis to say that elastase inhibitor III in the absence of KCN had no effect on cell viability. In fact, Figure 5B is evidence that elastase inhibitor III alone effects cell survival since it decreases survival from 100% to ~90%.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 10/5/09 and 9/18/09 have been considered by the examiner. It is noted that the IDS of 10/5/09 and 9/18/09 are identical as they include a single npl reference Henka and O'Banion.

It is noted that in the reply of 12/19/09 (page 9) that applicants refer to various references and state that an IDS will be submitted next week. No IDS was submitted within a week of 12/19/09.

Claim Rejections - 35 USC § 112

The 112 rejections are necessitated by applicants amendments.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 recites the limitation "the one or more elastase inhibiting agents" in claim 1. There is insufficient antecedent basis for this limitation in the claim. Claim 1 as amended recites 'elastase inhibiting agent'. Thus there is insufficient antecedent basis for 'the one or more elastase inhibiting agents'.

Although unclear, claim 3 has been interpreted as referring to the elastase inhibiting agent of claim 1.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 18,21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 18 recites 'wherein the amount of elastase inhibiting agent is less than the optimal amount for inhibiting necrosis when an anti-apoptotic agent is not used'.

Claim 21 recites 'wherein said elastase inhibiting agent is capable of .... inhibiting an enzyme acting in the cells undergoing necrosis'.

Lack of Ipsis Verbis Support

The specification is void of any literal support for a less than optimal amount of the elastase inhibiting agent.

The specification is void of any literal support for inhibiting any enzyme acting in the cells.

Lack of Implicit or Inherent Support

Section 2163 of the MPEP states: 'While there is no in haec verba requirement, newly added claim limitations must be supported in the specification through express, implicit, or inherent disclosure'.

The specification (page 10) states that the dosage can be varied and that an anti-apoptotic agent can be used. However, stating that the dosage can be varied would not lead one to 'amount of elastase inhibiting agent is less than the optimal amount for inhibiting necrosis when an anti-apoptotic agent is not used'. There is no basis for using a less than optimal amount. There is no direction in the specification to use less than optimal amounts. One would not conclude that there is support for using a less than optimal amount.

The specification (abstract) refers to inhibiting an elastase enzyme within cells. However, claim 21 is much broader as it recites 'inhibiting an enzyme acting in the cells'. While there is support for elastase inhibiting enzymes there is not support for inhibiting any and all enzymes. In other words, the phrase 'inhibiting an enzyme' is much broader than the phrase 'inhibiting an elastase enzyme'. There is no direction in the specification as to what other enzymes can be inhibited. One would not conclude that there is support for inhibiting any and all types of enzymes in the cells.

Claim Rejections - 35 USC § 102

Claims were previously rejected based on Gyorkos et al (US 6,001,813). Since the claims have been amended and new claims have been added the rejection is updated.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1,21 are rejected under 35 U.S.C. 102(b) as being anticipated by Gyorkos et al (US 6,001,813, first cited with office action 9/7/07).

Gyorkos et al. teach a method of administering an elastase inhibitor to a host in need thereof by using specific compounds (claim 10-11). Thus Gyorkos teach the active step as recited in claims 1,21. Gyorkos teach that the inhibitors are useful for the treatment of conditions including Alzheimer's disease (abstract and column 1 line 55) which is a form of dementia which meets the patient population of the instant claims (i.e. neurodegenerative disorder associated with necrosis). Gyorkos teach the use of an effective amount of the inhibitor (claim 10). Gyorkos teach that the diseases are human diseases (column 1 line 42) and teach human treatment (column 3 line 10). Since humans have neuronal cells the limitations as recited in claims 1,21 are met. It is noted that claims 1,21 recite that the inhibiting agent is capable of entering cells and claim 21 recites inhibiting an enzyme acting in the cells. First, it is noted that the claims recite 'capable of' and do not specify under what specific conditions. Gyorkos teach a variety of compositions for various administrations of the inhibitor (column 5 line 25-column 6

line 36). Further it is noted that Gyorkos expressly teach that the inhibitors are elastase inhibitors (claim 12) thus there is a reasonable basis, absence evidence to the contrary, that the inhibitors of Gyorkos are capable of entering cells. It is noted that 'necrosis' is defined on page 7 of the specification.

Response to Arguments 102 rejection

Since the claims have been amended, a new rejection adapted to the claims is recited above using the same reference as in the previous rejection. Applicants arguments will be considered to the extent that they apply to the current rejection and claim set.

Applicants argue (9/18/09 pages 5-7 and 12/19/09 pages 6-7) that human neutrophil elastase is the only proteinase for the inhibition of which there is enabling support in Gyorkos

Applicants argue that the mention of Alzheimers disease relates to a different proteinase.

Applicants argue that the claims recite inhibiting agent is capable of entering cells.

Applicants argue that example 7 pages 16-17 shows an impermeable inhibitor.

Applicants argue that the use of the tripeptides of Gyorkos are not obvious.

Applicant's arguments filed 9/18/09 and 12/19/09 have been fully considered but they are not persuasive.

Although Applicants argue that human neutrophil elastase is the only proteinase for the inhibition of which there is enabling support in Gyorkos, section 2121 of the MPEP states that prior art is presumed to be enabling and the burden is on the applicant to provide facts rebutting the presumption of operability. In the instant case, the active method step as claimed is administering an elastase inhibiting agent which is taught by Gyorkos.

Although Applicants argue that the mention of Alzheimers disease relates to a different proteinase, Gyorkos expressly teach administering elastase inhibitors (claims 10,12) using the compounds of claim 1 (see also Table I column 4) for the treatment of Alzheimers (abstract). Further, applicants own original claim 5 and election of species is evidence that Alzheimers is associated with cell necrosis.

Although Applicants argue that the claims recite inhibiting agent is capable of entering cells, it is first noted that the claims merely recite 'capable of' thus as claimed the agent is not required to enter the cells. There is no specificity provided as to how or under what conditions the agent can be tested to determine if it is capable of entering said cells. The claims do not require that the administration be in any particular manner or that the administration be to any particular location. The specification provides no direction as to the distinguishing features of agents capable of entering cells. The instant claims recite elastase inhibiting agent which is taught by the prior art. There is a reasonable basis that elastase inhibiting agents inhibit elastase. Please note, since the Office does not have the facilities for examining and comparing Applicants' composition with the composition of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. *See In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald*, 619 F.2d 67, 205 USPQ 594 (CCPA 1980), and "as a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith." *In re Brown*, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972).

Although Applicants argue that example 7 pages 16-17 shows an impermeable inhibitor, section 2145 I of the MPEP states that an assertion of what follows from common experience is just attorney argument and no the kind of factual evidence to overcome a rejection. Figure 7 appears to show effects of using different agents. Although one of the agents is asserted to be non permeable, the distinguishing features of a non permeable agent are not set forth nor has evidence been provided to verify that it is in fact non permeable. Although the specification states that no effect was seen there is no evidence to relate any effects to the properties of the inhibitor. In other words, there are many possible reasons why one inhibitor may not work while another may. In the instant case, Gyorkos expressly teach administering elastase inhibitors (claims 10,12) using the compounds of claim 1 (see also Table I column 4) for the treatment of Alzheimers (abstract). Applicants example 7 is not evidence that the compounds of Gyorkos do not function in the manner claimed.

Although Applicants argue that the use of the tripeptides of Gyorkos are not obvious, the instant rejection is a 102 rejection. The obviousness rejection (103 rejection) is discussed below.

Claim Rejections - 35 USC § 103

Claims were previously rejected based on Gyorkos et al. (US 6,001,813), and Stein et al. (Biochemistry 1986 v25 5414-5419). Since the claims have been amended and new claims have been added an updated rejection appears below.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1,21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gyorkos et al. (US 6,001,813, first cited with office action 9/7/07), and Stein et al. (Biochemistry 1986 v25 5414-5419, first cited with office action 9/7/07).

As discussed above, Gyorkos et al. teach a method of administering an elastase inhibitor to a host in need thereof by using specific compounds (claim 10-11). Thus Gyorkos teach the active step as recited in claims 1,21. Gyorkos teach that the inhibitors are useful for the treatment of conditions including Alzheimer's disease (abstract and column 1 line 55) which is a form of dementia which meets the patient population of the instant claims (i.e. neurodegenerative disorder assoctation with necrosis).

Gyorkos does not expressly teach the elected elastase inhibitor, elastase inhibitor III. Gyorkos teach tripeptides as inhibitors (claim 1 and abstract).

Stein also teach elastase inhibitors (abstract). Stein specifically teach a chloromethyl ketone peptide (MeOSuc-Ala-Ala-Pro-Val-CH2Cl) as an elastase inhibitor (abstract) which is the elected species of the current invention. Stein teach that the peptide derived chloromethyl ketones are irreversible inhibitors (age 5414 first paragraph). One of skill in the art would have been motivated to substitute the chloromethyl ketone peptide disclosed by Stein for the tripeptide disclosed by Gyorkos because both are known elastase inhibitors and Stein teach that the peptide derived chloromethyl ketones have desired qualities such as being irreversible inhibitors of serine proteases (elastase is a serine protease). As such one would be motivated to treat the patient population of Gyorkos (those with Alzheimers) using the peptide of Stein. One would have had a reasonable expectation for success since the peptides used are known elastase inhibitors. The claims would have been obvious because the substitution of one known element (chloromethyl ketone elastase inhibitor (MeOSuc-Ala-Ala-Pro-Val-CH2Cl) of Stein) for another (tripeptides of Gyorkos) would have yielded predictable results to one or ordinary skill in the art at the time of the invention.

Gyorkos et al. teach a method of administering an elastase inhibitor to a host in need thereof by using specific compounds (claim 10-11). Thus Gyorkos teach the active step as recited in claims 1,21. Gyorkos teach that the inhibitors are useful for the treatment of conditions including Alzheimer's disease (abstract and column 1 line 55) which is a form of dementia which meets the patient population of the instant claims (i.e. neurodegenerative disorder associated with necrosis). Gyorkos teach the use of an effective amount of the inhibitor (claim 10). Gyorkos teach that the diseases are human diseases (column 1 line 42) and teach human treatment (column 3 line 10). Since humans have neuronal cells the limitations as recited in

claims 1,21 are met. It is noted that claims 1,21 recite that the inhibiting agent is capable of entering cells and claim 21 recites inhibiting an enzyme acting in the cells. First, it is noted that the claims recite 'capable of' and do not specify under what specific conditions. Gyorkos teach a variety of compositions for various administrations of the inhibitor (column 5 line 25-column 6 line 36). Further, Stein also teach elastase inhibitors (abstract) specifically the elected species. There is a reasonable basis that the elected species would have the recited function. It is noted that 'necrosis' is defined on page 7 of the specification.

Response to Arguments 103 rejection Gyorkos and Stein

Since the claims have been amended, a new rejection adapted to the claims is recited above using the same references as in the previous rejection. Applicants arguments will be considered to the extent that they apply to the current rejection and claim set.

Applicants argue (9/18/09 page 7,10 and 12/19/09 page 9) that the peptides of Gyorkos are specific for HNE which is not active in the brain.

Applicant's arguments filed 9/18/09 and 12/19/09 have been fully considered but they are not persuasive.

Although Applicants argue that the peptides of Gyorkos are specific for HNE which is not active in the brain, Gyorkos expressly teach elastase inhibitors in claim 11. Thus one would not be limited to a single specific inhibitor. Section 2121 of the MPEP states that prior art is presumed to be enabling and the burden is on the applicant to provide facts rebutting the presumption of operability. Since Stein teach that the peptide derived chloromethyl ketones are irreversible inhibitors (age 5414 first paragraph) one would be motivated to use the peptides of Stein. Further, section 2143.02 II of the MPEP states that obviousness does not require absolute

predictability. In the instant case, one would have a reasonable expectation of substituting an elastase inhibitor (of Stein) for an elastase inhibitor (of Gyorkos) since they are both elastase inhibitors. No factual evidence has been provided to overcome the rejection. It is noted that in the reply of 12/19/09 (page 9) that applicants refer to various references and state that an IDS will be submitted next week. No IDS was submitted within a week of 12/19/09.

Claims were previously rejected based on Gyorkos et al. (US 6,001,813), and Rohn et al (American Journal of Pathology v158(2) Jan 2001 pages 189-198). Since the claims have been amended and new claims have been added an updated rejection appears below.

Claims 1,3,18,21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gyorkos et al. (US 6,001,813, first cited with office action 9/7/07), and Rohn et al (American Journal of Pathology v158(2) Jan 2001 pages 189-198, first cited with office action 3/18/09).

As discussed above, Gyorkos et al. teach a method of administering an elastase inhibitor to a host in need thereof by using specific compounds (claim 10-11). Thus Gyorkos teach the active step as recited in claims 1,21. Gyorkos teach that the inhibitors are useful for the treatment of conditions including Alzheimer's disease (abstract and column 1 line 55) which is a form of dementia which meets the patient population of the instant claims (i.e. neurodegenerative disorder assoctation with necrosis).

Gyorkos does not expressly teach the further administration of an anti-apoptotic agent as recited in claims 3,18.

Gyorkos teach that the inhibitors are useful for the treatment of conditions including Alzheimer's disease (abstract and column 1 line 55) which is a form of dementia.

Rohn also provide teachings regarding Alzheimers disease. Rohn teach that the results provide evidence that there is an association between neurofibrillary tangles (NFTs) and the activation of apoptotic pathways in Alzheimer's disease (abstract). Rohn teach that preventing caspase activation is one aspect of neurodegeneration amenable to therapeutic intervention (page 197 last paragraph). Rohn specifically teach the use of z-FAD-fmk (page 190 materials section) as a caspase inhibitor (page 192, Figure 1c). Rohn teach that treatment with caspase inhibitor z-FAD-fmk showed the involvement of caspases in the neurodegenerative process (page 193 first complete paragraph). Since both Gyorkos and Rohn are drawn to therapeutic intervention of Alzheimers it naturally flows to combine the individual teachings of the prior art. In the instant case one would be motivated to administer to those with Alzheimers both the elastase inhibitor as taught by Gyorkos and the anti-apoptotic agent (specifically z-FAD-fmk, a caspase inhibitor) as taught by Rohn. One would have a reasonable expectation of success since both are taught to have beneficial effects against Alzheimers. In the instant case the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

Gyorkos et al. teach a method of administering an elastase inhibitor to a host in need thereof by using specific compounds (claim 10-11). Thus Gyorkos teach the active step as recited in claims 1,21. Since Rohn motivate the use of an anti-apoptotic agent one would be

motivated to carry out the active steps of claims 3 and 18. Gyorkos teach that the inhibitors are useful for the treatment of conditions including Alzheimer's disease (abstract and column 1 line 55) which is a form of dementia which meets the patient population of the instant claims (i.e. neurodegenerative disorder associated with necrosis). Gyorkos teach the use of an effective amount of the inhibitor (claim 10). Gyorkos teach that the diseases are human diseases (column 1 line 42) and teach human treatment (column 3 line 10). Since humans have neuronal cells the limitations as recited in claims 1,21 are met. It is noted that claims 1,21 recite that the inhibiting agent is capable of entering cells and claim 21 recites inhibiting an enzyme acting in the cells. First, it is noted that the claims recite 'capable of' and do not specify under what specific conditions. Gyorkos teach a variety of compositions for various administrations of the inhibitor (column 5 line 25-column 6 line 36). Further it is noted that Gyorkos expressly teach that the inhibitors are elastase inhibitors (claim 12) thus there is a reasonable basis, absence evidence to the contrary, that the inhibitors of Gyorkos are capable of entering cells. It is noted that 'necrosis' is defined on page 7 of the specification.

It would have been obvious to one skilled in the art at the time of invention to determine all optimum and operable conditions (e.g. amounts of the agents), because such conditions are art-recognized result-effective variables that are routinely determined and optimized in the art through routine experimentation. ("[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). *See* MPEP § 2144.05). Thus one would be motivated to optimize the amount of the elastase inhibitor and anti-apoptotic agent as recited in claim 18.

It is noted that claims 3 and 18 state 'cause partial conversion of necrosis to apoptosis'. Since the prior art obviate the active steps (i.e. administration) using the claimed elements (elastase inhibitor and anti-apoptotic agent) the claim limitations are met obvious evidence to the contrary.

Although unclear (see 112 2nd), claim 3 has been interpreted as referring to the elastase inhibiting agent of claim 1.

Response to Arguments 103 rejection Gyorkos and Rohn

Since the claims have been amended, a new rejection adapted to the claims is recited above using the same references as in the previous rejection. Applicants arguments will be considered to the extent that they apply to the current rejection and claim set.

Applicants argue (9/18/09 pages 10-11) that the method of Gyorkos would not have any effect.

Applicants argue that synergistic results are achieved.

Applicant's arguments filed 9/18/09 and 12/19/09 have been fully considered but they are not persuasive.

Although Applicants argue that the method of Gyorkos would not have any effect, Section 2121 of the MPEP states that prior art is presumed to be enabling and the burden is on the applicant to provide facts rebutting the presumption of operability. Gyorkos et al. teach a method of administering an elastase inhibitor to a host in need thereof by using specific compounds (claim 10-11). Thus Gyorkos teach the active step as recited in claims 1,21. Gyorkos

teach that the inhibitors are useful for the treatment of conditions including Alzheimer's disease (abstract and column 1 line 55)

Although Applicants argue that synergistic results are achieved, section 2145 I of the MPEP states that an assertion of what follows from common experience is just attorney argument and no the kind of factual evidence to overcome a rejection. Further, section 716.02 of the MPEP states that the evidence must show unexpected results. In the instant claims it appears that the synergistic results are an assertion. Applicants point to no data and there appears to be no data of record relating to synergistic results.

Prior art of record

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure:

Proskuryakov et al (cited in IDS 3/14/08) teach (table I) that Alzheimers disease is associated with necrotic cell death of neurons.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to RONALD T. NIEBAUER whose telephone number is (571)270-3059. The examiner can normally be reached on Monday-Thursday, 7:30am-5:00pm, alt. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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